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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

T.H

Office Action Summary	Application No.	Applicant(s)	
	10/517,421	LUNDGREN-AKERLUND, EVY	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-8,13-16,19,20,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12,17-18,21 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-24 are pending.

2. A clear and obvious error occurs in the restriction wherein claim 23 was included in Group V. Claim 23 depends from claim 5, which was placed in Groups III and IV. Accordingly, claim 23 belongs to Groups III and IV. Further, claim 18, was not included in the Grouping. However, claim 18 belongs to elected Group V

3. Applicant's election with traverse of Group V, claims 9-12, 17-18, 21 and 24 directed to a method for detecting atherosclerotic plaque comprising determine the amount of integrin alphal0 chain filed on 9/22/06, is acknowledged.

Applicant's traversal is on the grounds that the present application is a national phase application under 37 C.F.R.§ 371 and the claims are united by the single inventive concept of the use of integrin alphal0 chain in the detection or treatment of atherosclerosis. This is not found persuasive because the different methods of Groups I-VI differ with respect to the biological end results (detection versus treatment). A disclosure of one method would not teach or suggest the other. Contrary to Applicant's assertions that all are united by the use of integrin alphal0 chain, the different Groups I-IV do not have a common core structure or function. For example Group I uses "agents" that binds to α10, Group II uses "nucleic acids", Groups III-VI fail to set forth an agent that would determine the amount of integrin α10 chain.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-8, 13-16, 19-20 and 22-23 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 9-12, 17-18, 21 and 24 are under examination as they read on a method for detecting atherosclerotic plaque comprising determine the amount of integrin alphal0 chain.

5. Claim 12, line 4, is objected for the following informalities: the recitation "of" after "said" is improper. Correction is required.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 9-12, 17-18, 21 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The method of claim 9 is indefinite because while all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The minimum requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized, and a correlation step describing how the results of the assay allow for the determination. Instant claim 9 fails to include a contacting step in which the reaction of the sample with the reagents necessary for the assay.

B. The recitation "further comprising contacting..." in claim 12 is indefinite because it is unclear whether the claim defined the determining step of claim 9(a) or adding a new step.

C. Claims 17-18 provide for the use of alpha10 chain, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 9-12, 17-18, 21 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide **enablement** for a method for detecting atherosclerotic plaque in a mammal comprising a) determining the amount of integrin alpha10 chain in a mammal, b) scoring the amount of integrin alpha10 chain in said mammal, relative to a control, and correlating the amount obtained in step b with amounts obtained from the control to detect said atherosclerotic plaque in the mammal in claim 9, wherein the determining is performed in vivo in claim 10 or in vitro in claim 11, wherein determining of the amount of integrin alpha10 chain further comprises contacting integrin alpha10 chain with a binding agent having a binding site specific for said integrin alpha10 chain in claim 12 or a method for diagnosing atherosclerotic comprising utilizing integrin alpha10 chain in claim 17 or a method for detecting atherosclerotic plaque comprising utilizing integrin alpha10 chain in claim 18, wherein the mammal is a human in claim 21 or mouse in claim 24. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification under example 1 discloses detection of the integrin alpha10 chain in aortic atherosclerotic plaque. The specification on page 18, under Results and discussion, discloses the detection of integrin alpha10 expression in the aortic plaques as strong around the outside of the cells in the aortic plaque (Fig.2A). Fig. 2b and 2c were controls to show the specificity of the antibody. However, the specification fails to show a differential expression or a correlation of α10 chain in atherosclerotic artery compared to normal artery for the method to be useful to detect atherosclerotic plaque. Lehnert et al (Cytogenet Cell Genet. 87:238-244, 1999) teaches that the expression pattern of integrin α10 subunit were widely expressed in a panel of 24 tissue types where the highest expression was found in muscle and heart (see abstract and Fig.5). Accordingly, in the absence of differential expression of alpha10 chain, a strong staining around the outside of the cells in the aortic plaque does not indicate that alpha10 is limited in its expression to the plaque and therefore, can be used as a marker for atherosclerotic plaque. While alpha10 chain is present in atherosclerotic plaque, little is known about the presence of alpha10 chain subunit at the normal site of the arteries of nonatherosclerotic sample. It is unclear whether alpha10 chain expression is present in both the normal nonatherosclerotic artery and in sites of atherosclerotic plaques or only at the site of atherosclerotic plaques. Importantly, WO 99/51639 publication teaches that analysis of the hybridized mRNA showed that α10 was expressed in aorta (normal nonatherosclerotic artery) (see pg. 25, lines 18-19 and Figure 12). Since the specification fail to demonstrate a differential expression between normal and atherosclerotic plaque aorta, the clinical value of Applicant's strategies is ineffective for detecting atherosclerotic plaque in vivo and in vitro.

Besides anti-alpha10 specific antibodies, the specification fails to provide any guidance as to how to make and how to use any "binding agent" for *in vitro* or *in vivo* detection of atherosclerotic plaque.

Applicant has not provided sufficient biochemical information that distinctly identifies such "binding agent" other than the anti-alpha10 antibodies. While any "binding agent" may have some notion of "integrin alpha10 chain recognition", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such agents, commensurate in scope with the claimed invention. The specification fails to provide any guidance on how to make binding agent that can be used for *in vitro* or *in vivo* detection of atherosclerotic plaque in a mammal. While the specification identifies some broad categories of compounds that *might* work, these descriptions, without more precise guidelines amount to little more than, "a starting point, a direction for further research." *Genentec, Inc. V.*

Novo Nordisk A/S, 108 F.3d 1361, 1366, 42 U.S. PQ.2d (BNA) 1001, 1005 (Fed. Cir. 1997).

Further, it is unclear what imaging device and imaging tag can be used to detect atherosclerotic plaque *in vivo* setting using the claimed binding agent having a binding site specific for integrin alpha10 chain. It is unclear what is the control for the *in vivo* method. Is the control for the *in vivo* method is another healthy nonatherosclerotic patient? I*n re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. No animal model system is used to detect atherosclerotic plaque *in vivo*. Since the method for detecting atherosclerotic plaque indices of administering to the mammal a binding agent can be species- and model-dependent, it is not clear that reliance on the in vitro studies accurately reflects the relative human detection strategy. It is not clear that the skilled artisan could predict the binding agent exemplified in the specification to detect atherosclerotic plaque in mammal *in vivo*.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. Claims 9-12, 17-18, 21 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of a method for detecting atherosclerotic plaque in a mammal comprising a) determining the amount of integrin alpha10 chain in a mammal, b) scoring the amount of integrin alpha10 chain in said mammal, relative to a control, and correlating the amount obtained in step b with amounts obtained from the control to detect said atherosclerotic plaque in the mammal in claim 9, wherein the determining is performed in vivo in claim 10 or in vitro in claim 11, wherein determining of the amount of integrin alpha10 chain further comprises contacting integrin alpha10 chain with a binding agent having a binding site specific for said integrin alpha10 chain in claim 12 or a method for diagnosing atherosclerotic comprising utilizing integrin alpha10 chain in claim 17 or a method for detecting atherosclerotic plaque comprising utilizing integrin alpha10 chain in claim 18, wherein the mammal is a human in claim 21 or mouse in claim 24.

Applicant has disclosed only anti-alpha10 antibody; therefore, the skilled artisan cannot envision all the contemplated binding agent possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be

satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/51639.

The `639 publication teaches that the isolated integrin subunit alpha10 can be used as a marker or target molecule for cells during pathological conditions such as atherosclerosis (see page 9, lines 11-37 in particular).

The reference teachings anticipate the claimed invention.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 9, 11-12 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/51639 in view of US. Pat. No. 6,458,590.

The `639 publication teaches that the isolated integrin subunit alpha10 can be used as a marker or target molecule for cells during pathological conditions such as atherosclerosis (see page 9, lines 11-37 in particular). Further, the `639 publication teaches that as a marker or target molecule of cells or tissues expressing said integrin subunit α10, which cells or tissues are of animal including human origin (see page 7, lines 30-33 in particular). Finally, the `639 publication teaches immunohistochemical staining of α10 in different tissues using the polyclonal antibody against the cytoplasmic domain as primary antibody (see Example 6) and a secondary antibody conjugated to peroxidase (see Example 11 on pg. 25 in particular).

The claimed invention differs from the reference teachings only by the recitation of a control in claim 9.

The `590 patent teaches that the data unambiguously demonstrate (a) expression of αvβ3 integrin protein in CASMCs in the arteries of control and atherosclerotic patients [as detected by immunofluorescence], (b) remarkable elevation in the expression of OPN-mRNA [as detected by in situ hybridization and RT-PCR] and OPN protein [as detected by visual inspection and densitometric analysis of Western blots] in CASMCs in the arteries of patients suffering from coronary atherosclerosis as compared to healthy individuals, (c) remarkable sustained elevation of OPN protein levels in the serum of arterial atherosclerotic patients following DCA procedure as compared to the levels in healthy controls and to atherosclerotic patients who did not undergo DCA (see col. 24, lines 47-60 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to perform a control as taught by `590 patent in the method of detecting atherosclerotic plaque taught by the `639 publication. Further, the `639 publication taught performing control implicitly because in order for a10 to be a marker for atherosclerosis, α10 must be compared to a control.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because to compared to the levels in healthy controls and to atherosclerotic patients as taught by the `590 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 30, 2006

Maher Haddad

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